

Sequence Listing

<110> Henry B. Lowman, Leonard G. Presta, Paula M. Jardieu, John Lowe
5 <120> Anti-IgE Antibodies and Method of Improving Polypeptides
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10 <140> US 09/109,207
 <141> 1998-06-30

15 <150> US 60/051,554
 <151> 1997-07-03

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 35 40 45
 40 Leu Glu Trp Met Gly Ser Ile Thr Tyr Asp Gly Ser Ser Asn Tyr
 50 55 60
 Asn Pro Ser Leu Lys Asn Arg Ile Ser Val Thr Arg Asp Thr Ser
 65 70 75
 45 Gln Asn Gln Phe Phe Leu Lys Leu Asn Ser Ala Thr Ala Glu Asp
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 50 Thr Ala Thr Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
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 Trp His Phe Ala Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser
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5 <223> F(ab) sequence derived from MAE11

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20 25 30

15 Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
35 40 45

Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
50 55 60

20 Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
65 70 75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

25 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
95 100 105

30 Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
110 115 120

Ser

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<213> Homo sapiens

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Ser Asp Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
35 40 45

55 Leu Glu Trp Val Ala Val Ile Ser Asn Gly Ser Asp Thr Tyr Tyr
50 55 60

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
65 70 75

60 Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Arg Phe Phe Xaa Xaa
 95 100 105

5 Xaa Xaa Xaa Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
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Ser

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 20 25 30

Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 35 40 45

25

Gln Pro Pro Ile Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Gly Ser
 50 55 60

30

Glu Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 65 70 75

Thr Leu Asn Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Phe
 80 85 90

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Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Ala Gly
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Thr Lys Leu Glu Ile Lys
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Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
 20 25 30

Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
 35 40 45

60

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
 50 55 60

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			80					85					90		
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20 25 30

5 Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
35 40 45

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
50 55 60

10 Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
65 70 75

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
80 85 90

15 Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
95 100 105

20 Thr Lys Val Glu Ile Lys Arg Thr Val
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<210> 9
<211> 114
<212> PRT
25 <213> Artificial

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<221> Artificial
<222> 1-114
30 <223> Light chain sequence derived from MAE11

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35 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
20 25 30

40 Tyr Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
35 40 45

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
50 55 60

45 Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
65 70 75

50 Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
80 85 90

Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
95 100 105

55 Thr Lys Val Glu Ile Lys Arg Thr Val
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<210> 10
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<220>

<221> Artificial
<222> 1-114
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20 25 30

Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
35 40 45

15 Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
50 55 60

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
20 65 70 75

20 Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
80 85 90

25 Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
95 100 105

Thr Lys Val Glu Ile Lys Arg Thr Val
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30 <210> 11
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35 <220>
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<222> 1-114
<223> Heavy chain sequence derived from MAE11

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20 25 30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
35 40 45

50 Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
50 55 60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
65 70 75

55 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

60 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
95 100 105

Trp His Phe Ala Val Trp Gly Gln Gly

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10 <222> 1-114

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35 40 4525 Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
50 55 60Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
65 70 7530 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
95 100 10535 Trp His Phe Ala Val Trp Gly Gln Gly
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45 <222> 1-218

<223> Light chain sequence derived from MAE11

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35 40 45Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
50 55 6060 Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
65 70 75

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	Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Val	Ser	Gly	Tyr	Ser	Ile	Thr
							20			25			30		
50	Ser	Gly	Tyr	Ser	Trp	Asn	Trp	Ile	Arg	Gln	Ala	Pro	Gly	Lys	Gly
							35			40			45		
	Leu	Glu	Trp	Val	Ala	Ser	Ile	Thr	Tyr	Asp	Gly	Ser	Thr	Asn	Tyr
							50			55			60		
55	Asn	Pro	Ser	Val	Lys	Gly	Arg	Ile	Thr	Ile	Ser	Arg	Asp	Asp	Ser
							65			70			75		
	Lys	Asn	Thr	Phe	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp
60							80			85			90		
	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Gly	Ser	His	Tyr	Phe	Gly	His
							95			100			105		

	Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser		
	110	115	120
5	Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser		
	125	130	135
	Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val		
	140	145	150
10	Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly		
	155	160	165
15	Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser		
	170	175	180
	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser		
	185	190	195
20	Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro		
	200	205	210
	Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp		
	215	220	225
25	Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
	230	235	240
30	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu		
	245	250	255
	Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val		
	260	265	270
35	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
	275	280	285
	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr		
	290	295	300
40	Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln		
	305	310	315
45	Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
	320	325	330
	Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
	335	340	345
50	Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu		
	350	355	360
	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly		
	365	370	375
55	Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln		
	380	385	390
60	Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp		
	395	400	405
	Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg		

	410	415	420	
	Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala			
	425	430	435	
5	Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly			
	440	445	450	
	Lys			
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25	Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp			
	20	25	30	
	Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly			
30	35	40	45	
	Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser			
	50	55	60	
35	Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe			
	65	70	75	
	Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr			
40	80	85	90	
	Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly			
	95	100	105	
	Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe			
45	110	115	120	
	Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser			
	125	130	135	
50	Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val			
	140	145	150	
	Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu			
55	155	160	165	
	Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser			
	170	175	180	
	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val			
60	185	190	195	
	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr			

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205

210

Lys Ser Phe Asn Arg Gly Glu Cys
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5

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Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
20 25 30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
35 40 45

25

Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
50 55 60

30

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
65 70 75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
80 85 90

35

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
95 100 105

40

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
110 115 120

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
125 130 135

45

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
140 145 150

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
155 160 165

50

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
170 175 180

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
185 190 195

55

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
200 205 210

60

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
215 220 225

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly

	230	235	240
	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu		
5	245 250	250	255
	Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val		
	260 265	265	270
10	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
	275 280	280	285
	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr		
	290 295	295	300
15	Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln		
	305 310	310	315
20	Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
	320 325	325	330
	Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
	335 340	340	345
25	Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu		
	350 355	355	360
	Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly		
	365 370	370	375
30	Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln		
	380 385	385	390
	Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp		
35	395 400	400	405
	Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg		
	410 415	415	420
40	Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala		
	425 430	430	435
	Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly		
	440 445	445	450
45	Lys		
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	Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp		

	20	25	30	
	Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly			
5	35	40	45	
	Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser			
	50	55	60	
10	Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe			
	65	70	75	
	Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr			
	80	85	90	
15	Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly			
	95	100	105	
	Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe			
20	110	115	120	
	Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser			
	125	130	135	
25	Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val			
	140	145	150	
	Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu			
	155	160	165	
30	Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser			
	170	175	180	
	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val			
35	185	190	195	
	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr			
	200	205	210	
40	Lys Ser Phe Asn Arg Gly Glu Cys			
	215			
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55	Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr			
	20	25	30	
60	Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly			
	35	40	45	
	Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr			

	50	55	60
	Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser		
	65	70	75
5	Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp		
	80	85	90
10	Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His		
	95	100	105
	Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser		
	110	115	120
15	Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser		
	125	130	135
	Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val		
	140	145	150
20	Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly		
	155	160	165
25	Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser		
	170	175	180
	Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser		
	185	190	195
30	Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro		
	200	205	210
	Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp		
35	215	220	225
	Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly		
	230	235	240
40	Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu		
	245	250	255
	Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val		
	260	265	270
45	Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly		
	275	280	285
	Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr		
50	290	295	300
	Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln		
	305	310	315
55	Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys		
	320	325	330
	Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
	335	340	345
60	Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu		
	350	355	360

	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly
							365			370				375	
5	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln
							380		385					390	
	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp
							395			400				405	
10	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg
							410		415					420	
	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala
15							425			430				435	
	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly
							440		445					450	
	Lys														
20															
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							20				25			30	
	Gly	Glu	Gly	Asp	Ser	Tyr	Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly
40							35			40				45	
	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Ala	Ala	Ser	Tyr	Leu	Glu	Ser
							50				55			60	
45	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe
							65			70				75	
	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr
50							80			85				90	
	Tyr	Cys	Gln	Gln	Ser	His	Glu	Asp	Pro	Tyr	Thr	Phe	Gly	Gln	Gly
							95			100				105	
	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe
55							110			115				120	
	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser
							125			130				135	
60	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val
							140			145				150	

	Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu			
	155	160	165	
5	Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser			
	170	175	180	
	Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val			
	185	190	195	
10	Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr			
	200	205	210	
	Lys Ser Phe Asn Arg Gly Glu Cys			
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15	<210> 20			
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	Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly			
	35	40	45	
35	Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr			
	50	55	60	
40	Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser			
	65	70	75	
	Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp			
	80	85	90	
45	Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His			
	95	100	105	
	Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser			
50	110	115	120	
	Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser			
	125	130	135	
55	Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val			
	140	145	150	
	Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly			
	155	160	165	
60	Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser			
	170	175	180	

	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser
															185
															190
															195
	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro
5															200
															205.
															210
	Ser	Asn	Thr	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys	Ser	Cys	Asp
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															220
															225
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	1				5						10				
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	20				25						30				
30	Ser	Gly	Tyr	Ser	Trp	Asn	Trp	Ile	Arg	Gln	Ala	Pro	Gly	Lys	Gly
	35				40						45				
	Leu	Glu	Trp	Val	Ala	Ser	Ile	Lys	Tyr	Ser	Gly	Glu	Thr	Lys	Tyr
35					50						55				60
	Asn	Pro	Ser	Val	Lys	Gly	Arg	Ile	Thr	Ile	Ser	Arg	Asp	Asp	Ser
	65				70						75				
40	Lys	Asn	Thr	Phe	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp
	80				85						90				
	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Gly	Ser	His	Tyr	Phe	Gly	His
	95				100						105				
45	Trp	His	Phe	Ala	Val	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser
	110				115						120				
	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser
50					125					130					135
	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val
	140				145					150					
	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly
55					155					160					165
	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser
	170				175					180					
60	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser
	185				190					195					

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 200 205 210
 5 Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 215 220 225
 Lys Thr His Thr

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25 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 20 25 30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
 35 40 45

30 Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
 50 55 60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 65 70 75

35 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
 80 85 90

40 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 95 100 105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 110 115 120

45 Ser Glu Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly
 125 130 135

Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
 140 145 150

50 Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val
 155 160 165

Asp Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
 55 170 175 180

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu
 185 190 195

60 Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
 200 205 210

	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr
					215					220					225
5	Tyr	Tyr	Cys	Gln	Gln	Ser	His	Glu	Asp	Pro	Tyr	Thr	Phe	Gly	Gln
					230				235						240
	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg							
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				20					25					30	
	Ser	Gly	Tyr	Ser	Trp	Asn	Trp	Ile	Arg	Gln	Ala	Pro	Gly	Lys	Gly
					35				40					45	
30	Leu	Glu	Trp	Val	Ala	Ser	Ile	Lys	Tyr	Ser	Gly	Glu	Thr	Lys	Tyr
					50				55					60	
	Asn	Pro	Ser	Val	Lys	Gly	Arg	Ile	Thr	Ile	Ser	Arg	Asp	Asp	Ser
35					65				70					75	
	Lys	Asn	Thr	Phe	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp
					80				85					90	
40	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Gly	Ser	His	Tyr	Phe	Gly	His
					95				100					105	
	Trp	His	Phe	Ala	Val	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser
					110				115					120	
45	Ser	Glu	Gly	Gly	Ser	Glu	Gly	Gly	Ser	Glu	Gly	Gly	Gly	Gly	Gly
					125				130					135	
	Ser	Asp	Ile	Gln	Leu	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser
50					140				145					150	
	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Lys	Pro	Val
					155				160					165	
55	Asp	Gly	Glu	Gly	Asp	Ser	Tyr	Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro
					170				175					180	
	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Ala	Ala	Ser	Tyr	Leu	Glu
					185				190					195	
60	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp
					200				205					210	

	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr
					215					220				225	
5	Tyr	Tyr	Cys	Gln	Gln	Ser	His	Glu	Asp	Pro	Tyr	Thr	Phe	Gly	Gln
					230			235			240				
	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg							
					245										
10	<210>	24													
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	<222>	1-218													
	<223>	Light chain F(ab)'2 sequence derived from MAE11													
20	<400>	24													
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	1		5							10				15	
25	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Lys	Pro	Val	Asp
					20				25				30		
	Gly	Glu	Gly	Asp	Ser	Tyr	Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly
					35				40				45		
30	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Ala	Ala	Ser	Tyr	Leu	Glu	Ser
					50				55				60		
	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe
35					65				70				75		
	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr
					80				85				90		
40	Tyr	Cys	Gln	Gln	Ser	His	Glu	Asp	Pro	Tyr	Thr	Phe	Gly	Gly	
					95				100				105		
	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe
					110				115				120		
45	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser
					125				130				135		
	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val
50					140				145				150		
	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	Glu
					155				160				165		
55	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser
					170				175				180		
	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val
					185				190				195		
60	Tyr	Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr
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Lys Ser Phe Asn Arg Gly Glu Cys
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20 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 20 25 30

25 Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
 35 40 45

30 Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
 50 55 60

35 Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 65 70 75

40 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
 80 85 90

45 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 95 100 105

50 Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 110 115 120

55 Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
 125 130 135

60 Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
 140 145 150

65 Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 155 160 165

70 Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
 170 175 180

75 Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 185 190 195

80 Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 200 205 210

85 Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 215 220 225

90 60 Lys Thr His Thr Cys Pro Pro Cys
 230

<210> 26
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 1 5 10 15
 15 Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 20 25 30
 Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
 20 35 40 45
 25 Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
 50 55 60
 30 Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 65 70 75
 Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
 80 85 90
 35 Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 95 100 105
 Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 35 110 115 120
 Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
 125 130 135
 40 Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
 140 145 150
 Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
 155 160 165
 45 Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
 170 175 180
 Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 50 185 190 195
 Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 200 205 210
 55 Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 215 220 225
 Lys Thr His Thr Cys Pro Pro Cys
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5 <221> Artificial
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<212> DNA
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15 <220>
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20 gccagtcaga gcgtctaata ataaggta agctacactga actgg 46

<210> 29
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40 <213> Artificial

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45 <223> Stop-Template Oligos For First-Round Mutagenesis

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50 <210> 31
<211> 53
<212> DNA
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55 <220>
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<222> 1-53
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60 <400> 31
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acc 53

<210> 32
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5 <212> DNA
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10 <222> 1-46
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<210> 35
45 <211> 48
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50 <221> Artificial
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<210> 37
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<400> 37
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45 <400> 38
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<210> 39
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55 <220>
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60 <220>
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5 <210> 40
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15 <220>
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acc 53

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35 <220>
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